



AF-1615
IFW

THE UNITED STATES PATENT AND TRADEMARK OFFICE
Re: Appeal to the Board of Appeals

In re Application of)
HEGER et al.)
Serial No. 09/857,480)
Filed: August 13, 2002)
For: NANOPARTICULATE CORE/SHELL SYSTEMS AND THE USE THEREOF IN
PHARMACEUTICAL AND COSMETIC PREPARATIONS
To: Hon. Commissioner of Patents and Trademarks

MAIL STOP APPEAL BRIEF

Art Unit: 1615

Examiner: Bennett

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3. ☒ BRIEF on appeal in this application is transmitted herewith.
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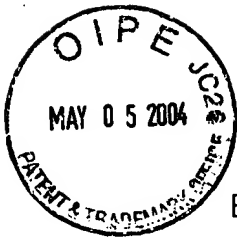
Respectfully submitted,
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re the application of

HEGER et al.

Serial No. 09/857,480

Filed: August 13, 2002

) **MAIL STOP APPEAL BRIEF**

)

) Group Art Unit: 1615

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) Examiner: Bennett

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BRIEF ON APPEAL

Sir:

This appeal is from the examiner's final rejection of October 31, 2003 and further in
response to the advisory action dated March 9, 2004. Appellants' Notice of Appeal was
filed on March 1, 2004.

REAL PARTY IN INTEREST

The real party in interest is BASF Aktiengesellschaft, of Ludwigshafen, Germany.

Reel/Frame 012057/0717, recorded on June 5, 2001.

RELATED APPEALS AND INTERFERENCES

To appellants' knowledge and belief, there are no interferences or other appeals which will directly affect or be directly affected by or have a bearing on the Board's decision in this application.

STATUS OF THE CLAIMS

Claims 15-25 remain in the application. Claims 15-18 are rejected under 35 USC § 103(a) as being unpatentable over Stainmesse et al. (US 5,133,908). Claims 15-18 and 22-25 are rejected under 35 USC § 103(a) as being unpatentable over List et al. (US 5,389,382). Claims 15-25 are rejected under 35 USC § 103(a) as being unpatentable over List et al. (US 5,389,382) in view of Liversidge et al. (US 5,145,684).

STATUS OF THE AMENDMENTS

The claims have not been amended subsequent to the examiner final office action dated October 31, 2003.

SUMMARY OF THE INVENTION

The present invention relates to nanoparticulate preparations of pharmaceutical active ingredients with a core/shell structure, where the active ingredient is present in the core in X-ray amorphous form together with at least one polymer, and the shell consists of a polymeric matrix.

ISSUES

Whether claims 15-18 are unpatentable under 35 USC § 103 as being obvious

over Stainmesse et al. (US 5,133,908).

Whether claims 15-18 and 22-25 are unpatentable under 35 USC § 103(a) as being obvious over List et al. (US 5,389,382).

Whether claims 15-25 are unpatentable under 35 USC § 103(a) as being obvious over List et al. (US 5,389,382) in view of Liversidge et al. (US 5,145,684).

GROUPING OF CLAIMS

The claims have not been argued separately.

ARGUMENT

The following legal authorities are relied on in the following arguments in the order in which they are cited:

In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988);

In re Jones, 958 F.2d 347, 21 USPQ 2d 1941 (Fed. Cir. 1992);

In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986);

In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)

THE REJECTIONS

The examiner has not met her burden to establish *prima facie* obviousness under 35 USC § 103(a). To establish *prima facie* obviousness, the examiner must show in the prior art some suggestion or motivation to make the claimed invention, a reasonable expectation for success in doing so, and a teaching or suggestion of each claim element (see, e.g., *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958

F.2d 347, 21 USPQ 2d 1941 (Fed. Cir. 1992); *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)).

Stainmesse et al. do not teach or suggest all the claim limitations of the rejected claims (15-18, 22-25). The examiner has not shown how the following limitation in the present rejected claims is taught or suggested by Stainmesse et al.: "...continuously in a mixing chamber **by spraying the two components as a compact jet into a mixing chamber.**" Therefore, the examiner has not set forth a *prima facie* case of obviousness.

The examiner also has not shown how there would be a reasonable expectation of success in modifying Stainmesse et al. to teach or suggest the claimed invention. Reasonable expectation of success is one of the requirements for establishing a *prima facie* case of obviousness.

Applicants also believe the examiner has not set forth an adequate motivation to modify the teachings in Stainmesse et al. Stainmesse et al. teaches that there is a need for moderate agitation dependent on the amounts utilized and no agitation is needed at all for smaller quantities (col. 4, lines 42-44). No person of ordinary skill in the art would be motivated to use "moderate agitation" for larger amounts to spray the two components as a compact jet into a mixing chamber. Proceeding contrary to the accepted wisdom of the prior art is strong evidence of nonobviousness. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303, 312, (Fed. Cir. 1993); *In re Hedges*, 783 F.2d 1038,

228 USPQ 685, 687 (Fed. Cir. 1986). In view of this, applicants further believe the examiner has not set forth a *prima facie* case of obviousness.

Claims 15-18, 22-25 are rejected under 35 USC § 103(a) as being unpatentable over List et al. (US 5,389,382). The examiner stated that absent unexpected results, it would have been obvious to one of ordinary skill in the art to have mixed the composition either in a batch, as suggested by List et al., or continuously, as both are well-known in the art. The examiner stated that both processes result in a precipitation, wherein the suspension or colloid is converted into a dry powder.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves, or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP § 2143.

Applicant believe the examiner not set forth a *prima facie* case of obviousness regarding List et al. First, the examiner also has not shown for this rejection how there would be a reasonable expectation of success in modifying List et al. to teach or suggest the claimed invention. Reasonable expectation of success is one of the requirements for establishing a *prima facie* case of obviousness.

Second, suggestion or motivation to modify List et al. to teach the elements of the

rejected claims is not present. List et al. only relate to batch-wise production of the particle. Therefore, one of ordinary skill in the art will recognize that batch-wise operation disclosed by List et al. has to be followed by filtration to separate any coarse particles. (see examples 1 and 2 of List et al.). This shows that the teaching in List et al. would not lead to fine particles with uniform size without further steps.

Also, even though it may be known in principle that processes can be operated continuously, one cannot necessarily infer that for a specific process, desired results to be achieved by a continuous process only if the batch wise mode of operation has been disclosed in the references. Therefore, one of ordinary skill in the art would not conclude from List et al. that a process as presently claimed will avoid the additional distinct step of separating coarse particles. Before obviousness may be established, the examiner must show that there is either a suggestion in the art to produce the claimed invention or a compelling motivation based on sound scientific principles. *Ex parte Kranz*, 19 USPQ2d 1216, 1218 (BPAI 1990).

Claims 15-25 are rejected under 35 USC § 103 (a) as being unpatentable over List et al. (US 5,389,382) in view of Liverside et al. (US 5,145,684). The examiner stated that absent unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the composition of List et al. by substituting casin as taught by Liverside for gelatin as the coating polymer because of the expectation of unexpected bioavailability and are useful in methods of treating mammals

as taught by Liversidge et al.

Applicants' above arguments regarding List et al. applies here as well.

The present invention is directed to a specific continuous process. The examiner relies on Liversidge et al. for the teaching of an alternative coating polymer and that the polymer coating taught by Liversidge et al. can be used for both crystalline and amorphous drugs. Applicants believe examiner's argument is inapplicable since the presently claimed invention is directed to a specific continuous process. The presently claimed process relies on the principle that an active ingredient is first dissolved and then precipitated to obtain a nanoparticulate form. According to Liversidge et al., the active ingredient is not dissolved at all. Reduction in particle size is achieved by wet-grinding of a polymeric slurry. Therefore, one of ordinary skill in the art would not combine the teachings of List et al. and Liversidge et al. to arrive at the claimed continuous process where the components are sprayed into the mixing chamber. Neither List et al. and Liversidge et al. teach anything regarding continuous operation of a process. Before obviousness may be established, the examiner must show that there is either a suggestion in the art to produce the claimed invention or a compelling motivation based on sound scientific principles. *Ex parte Kranz*, 19 USPQ2d 1216, 1218 (BPAI 1990).

For the reasons expressed above, it is urged that the prior art references cited by the examiner either singly or in combination fail to anticipate or suggest the present invention as defined by the amended claims. Accordingly, a *prima facie* case of

obviousness has not been established by the examiner, and the rejection under 35 USC § 103 should be withdrawn.

CONCLUSION

It is respectfully submitted that reversal of the of the examiner's rejection of all claims is in order. _____

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Respectfully submitted,

KEIL & WEINKAUF

A handwritten signature in black ink, appearing to read 'Dan Kim', is written over the printed name.

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APPENDIX

Claims 1-14 (canceled).

15. (previously presented) A process for preparing a nano-particulate preparation of a pharmaceutical or cosmetic active ingredient with a core/shell structure, in which the X-ray amorphous active ingredient is present in the core together with one or more polymers, and the shell consists of a stabilizing coating matrix, comprising mixing the active ingredient/polymer solution or precipitate with the aqueous solution of the polymeric coating material continuously in a mixing chamber by spraying the two components as a compact jet into a mixing chamber.

16. (previously presented) The process as claimed in claim 1, in which the core of the preparation has at least two separate phases, one phase consisting of amorphous particles of the active ingredient, and the other phase being a molecular dispersion of the active ingredient in a polymer matrix.

17. (previously presented) The process as claimed in claim 1, in which the core of the preparation has at least two separate phases, one phase consisting of amorphous active ingredient, and the other phase being a polymer matrix free of active ingredient.

18. (previously presented) The process as claimed in claim 1, wherein the core polymers are polymers which are suitable for pharmaceutical and cosmetic applications and which are insoluble or only partly soluble in water.

19. (previously presented) The process as claimed in claim 1, in which the preparation

comprises polymeric peptides as coating matrix.

20. (previously presented) The process as claimed in claim 1, in which the preparation comprises gelatin as coating polymer.

21. (previously presented) The process as claimed in claim 1, in which the preparation comprises casein or sodium caseinate as coating matrix.

22. (previously presented) The process as claimed in claim 1, in which the core/shell structures have an average particle diameter between 0.01 and 2 μm .

23. (previously presented) The process as claimed in claim 1, in which the said process produces a hydrosol of the said nanoparticulate preparation.

24. (previously presented) The process as claimed in claim 23, in which the sizes of the hydrosol nanoparticles increase by less than 50% in the first hour after preparation of the hydrosol.

25. (previously presented) A process for producing preparations as claimed in claim 1, which comprises preparing a solution of the active ingredient in an organic solvent which is at least 10% by weight miscible in water, mixing this solution with the core polymer or a solution of the core polymer in an organic solvent, and bringing the resulting mixture into contact with an aqueous solution of the coating polymer.